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| 10/075,593 | 02/15/2002 | Ellen M. Heath | 2902162-017000 | 9392 |

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| EXAMINER | |
|---|---|
| STRZELECKA, TERESA E | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/075,593 | HEATH ET AL. | |
| | Examiner | Art Unit | |
| | TERESA E. STRZELECKA | 1637 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *26 August 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-7,10-17,19-28,31-38,40-49,52-59 and 61-70* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *24-28,31-38,40-49,52-59 and 61-65* is/are allowed.

6)☒ Claim(s) *1-7,10-17,19-23 and 66-70* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

**DETAILED ACTION**

1. This office action is in response to an amendment filed August 26, 2009. Claims 1-7, 10-17, 19-28, 31-38, 40-49, 52-59 and 61-65 were previously pending. Applicants amended claims 1-3, 16, 24, 25, 37, 45 and 58, and added new claims 66-70. Claims 1-7, 10-17, 19-28, 31-38, 40-49, 52-59 and 61-70 are pending and will be examined.

2. Applicants' arguments overcame the following rejections: the rejection of claims 1-7, 10-17, 19-28, 31-38, 40-49, 52-59 and 61-65 under 35 U.S.C. 112, first paragraph, best mode; the rejection of claims 1-7, 10-17, 19-28, 31-38, 40-49, 52-59 and 61-65 under 35 U.S.C. 112, first paragraph, written description; the rejection of claims 1-7, 10-17, 19-28, 31-38, 40-49, 52-59 and 61-65 under 35 U.S.C. 112, first paragraph, enablement. Applicants' amendments overcame the rejection of claims 1-7, 10-17, 19-28, 31-38, 40-49, 52-59 and 61-65 under 35 U.S.C. 112, second paragraph.

3. The declaration of Dr. Dirk Loeffert under 37 CFR 1.132 filed August 26, 2009 is sufficient to overcome the rejection of claims 24, 25, 27, 28, 31-38, 40-44 under 35 U.S.C. 103(a) as being unpatentable over Laitinen et al.; rejection of claims 1-7, 10-16, 19-28, 31-37, 40-49, 52-58 and 61-65 under 35 U.S.C. 103(a) as being unpatentable over Fairman as evidenced by Shih et al. and Moskaitis et al.; and the rejection of claims 17, 38 and 59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fairman and Hanak et al.

4. All other previously presented rejections are maintained for reasons given in the "Response to Arguments" section below.

5. This office action is made non-final because of new grounds for rejection.

***Response to Arguments***

6. Applicant's arguments filed August 26, 2009 have been fully considered but they are not persuasive.

Regarding the rejection of claims 1-7, 10-17 and 19-23 under 35 U.S.C. 103(a) over Laitinen et al., Applicants argue that the declaration of Dr. Loeffert provides evidence of unexpected results obtained when cells are resuspended in high salt buffer before being lysed. While these arguments were persuasive with respect to the rejections based on resuspension of whole cells, they are not persuasive with respect to the Laitinen et al. reference and claims 1-7, 10-17 and 19-23, since these claims read on resuspension of "biological material comprising DNA", for example, nuclei, in high-salt solution, taught by Laitinen et al.. Since Applicants did not present any evidence of unexpected result with respect to cell nuclei, the rejection is maintained.

***Claim Rejections - 35 USC § 102***

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1-4, 6, 7, 10, 13-16, 19-23 and 66-70 are rejected under 35 U.S.C. 102(b) as being anticipated by Lahiri et al. (Nucl. Acids Res., vol. 19, p. 5444, 1991) as evidenced by Shih et al. (Biotechnol. Bioeng., vol. 40, pp. 1155-1164, 1992; cited in the previous office action) and Moskaitis et al. (Neurochem. Res., vol. 11, pp. 299-315, 1986; cited in the previous office action).

Regarding claims 1 and 2, Lahiri et al. teach a method of isolating DNA from a biological sample, the method comprising the following sequential steps:

(a) separating the biological material comprising DNA from the remainder of the biological sample (Lahiri et al. teach separating nucleic from the remainder of the cells (page 5444, second paragraph, steps 1-5).);

(b) contacting the separated biological material comprising DNA of step (a) with a hypertonic, high salt reagent so as to form a suspension of said biological material containing DNA (page 5444, second paragraph, step 6, where the nuclei are contacted with a high salt buffer with 0.4 M NaCl (=hypertonic salt reagent).);

(c) contacting the suspension of step (b) with a lysis reagent so as to lyse the biological material containing DNA to form a lysate comprising DNA and non-DNA biological components released from the biological material, wherein the said hypertonic, high-salt reagent in step (b) comprises salt in an amount effective to precipitate proteins out of the lysate (page 5444, second paragraph, step 7, where the nuclei are contacted with a lysis buffer. Since the final salt concentration is about 0.4 M, it is effective in precipitating proteins out of the lysate. As evidenced by Shih et al., protein precipitation depends both on ionic strength of solution and pH, therefore, about 0.4 M salt concentration would be effective in precipitating some of the proteins from the lysate, especially in the presence of subsequently added SDS, as evidenced by Moskaitis et al.); and

(d) separating the DNA from non-DNA biological components in the lysate to yield isolated DNA (page 5444, second paragraph, steps 8-10).

Regarding claims 3, 6 and 66-70, Lahiri et al. teach whole blood (page 5444, second paragraph, step 1).

Regarding claim 4, Lahiri et al. teach whole blood obtained from humans (page 5444, second paragraph, step 1; third paragraph). Since human blood inherently contains viruses, this limitation is anticipated.

Regarding claim 7, Lahiri et al. teach purifying DNA from the rest of the cell, which contain proteins, lipids, RNA and carbohydrates (page 5444, second paragraph, step 1-9).

Regarding claim 10, Lahiri et al. teach NaCl (page 5444, second paragraph, step 6).

Regarding claims 13-15, Lahiri et al. teach SDS (page 5444, second paragraph, step 7).

Regarding claim 16, Lahiri et al. teach SDS concentration of 10% (page 5444, second paragraph, step 7).

Regarding claims 19 and 20, Lahiri et al. teach mixing the samples and centrifuging the lysate (page 5444, second paragraph, step 8-9).

Regarding claim 21, Lahiri et al. teach precipitating the DNA with alcohol (page 5444, second paragraph, step 11).

Regarding claim 22, Lahiri et al. teach washing the DNA pellets (page 5444, second paragraph, step 12).

Regarding claim 23, Lahiri et al. teach treating DNA with a hydration reagent (page 5444, second paragraph, step 14).

***Claim Rejections - 35 USC § 103***

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 11 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lahiri et al. (Nucl. Acids Res., vol. 19, p. 5444, 1991).

Regarding claims 11 and 12, Lahiri et al. teach a concentration of 0.4 M NaCl, but do not teach 1 or 2 M NaCl.

However, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to adjust the concentration of NaCl in the high salt buffer of Lahiri et al. to a desired level. Thus, an ordinary practitioner would have recognized that optimizable variable of salt concentration could be adjusted to maximize the desired results. As noted in *In re Aller*, 105 USPQ 233 at 235,

> More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.

Routine optimization is not considered inventive and no evidence has been presented that the selection of specific salt concentration was other than routine, that the products resulting from the optimization have any unexpected properties, or that the results should be considered unexpected in any way as compared to the closest prior art.

11. Claims 1-7, 10-17, 19-23 and 66-70 are rejected under 35 U.S.C. 103(a) as being unpatentable over Laitinen et al. (Biotechniques, vol. 17, pp. 316, 318, 320-322, 1994).

A) Claims 1 and 2 will be considered together in claim 1, since it is a species of claim 2.

Regarding claims 1 and 2, Laitinen et al. teach a method of isolating DNA from a biological sample comprising red and white blood cells, the method comprising the following sequential steps:

(a) separating the biological material comprising DNA from the remainder of the biological sample (Laitinen et al. teach separating nucleic from the remainder of the cells (page 316, sixth paragraph).);

(b) contacting the separated biological material comprising DNA of step (a) with a hypertonic, high salt reagent having a concentration of salt therein, so as to form a suspension of said biological material containing DNA (page 316, sixth paragraph, where the nuclei are contacted with a lysis buffer and 5 M NaCl (=hypertonic salt reagent).);

(c) contacting the suspension of step (b) with a lysis reagent so as to lyse the biological material containing DNA to form a lysate comprising DNA and non-DNA biological components released from the biological material, wherein the said hypertonic, high-salt reagent in step (b) comprises salt in an amount effective to precipitate proteins out of the lysate (page 316, sixth paragraph, where the nuclei are contacted with a lysis buffer and 5 M NaCl (=hypertonic salt reagent). Since the final salt concentration is 1.2 M, it is effective in precipitating proteins out of the lysate.); and

(d) separating the DNA from non-DNA biological components in the lysate to yield isolated DNA (page 316, sixth paragraph).

Regarding claims 3 and 66-70, Laitinen et al. teach verterbrate tissues, blood cells and bacterial cells (page 316, fourth paragraph).

Regarding claim 4, Laitinen et al. teach buffy coats (page 316, fourth paragraph). Since buffy coats are obtained from whole blood, Laitinen et al. inherently teach whole blood. Since human blood inherently contains viruses, this limitation is anticipated.

Regarding claim 5, Laitinen et al. do not specifically teach cells from bone marrow, but since they teach several different types of cells, it would have been prima facie obvious to apply the method of Laitinen et al. to isolation of DNA from any other type of cell, including bone marrow.

Regarding claim 6, Laitinen et al. teach buffy coats (page 316, fourth paragraph). Since buffy coats are obtained from whole blood, Laitinen et al. inherently teach whole blood.

Regarding claim 7, Laitinen et al. teach purifying DNA from the rest of the cell, which contain proteins, lipids, RNA and carbohydrates (page 316, sixth paragraph).

Regarding claim 10, Laitinen et al. teach NaCl (page 316, sixth paragraph).

Regarding claims 11 and 12, Laitinen et al. teach NaCl solution with 5 M concentration (page 316, sixth paragraph).

Regarding claims 13-15, Laitinen et al. teach SDS (page 316, sixth paragraph).

Regarding claim 16, Laitinen et al. teach SDS concentration of 1% (page 316, sixth paragraph).

Regarding claim 17, Laitinen et al. teach RNAse (page 316, sixth paragraph).

Regarding claims 19 and 20, Laitinen et al. teach vortexing the samples and centrifuging the lysate (page 316, sixth paragraph).

Regarding claim 21, Laitinen et al. teach precipitating the DNA with alcohol (page 316, sixth paragraph).

Regarding claim 22, Laitinen et al. teach washing the DNA pellets (page 318, first paragraph).

Regarding claim 23, Laitinen et al. teach treating DNA with a hydration reagent (page 316, sixth paragraph).

B) Laitinen et al. do not teach contacting the nucleic first with the high salt reagent.

However, the final result of step c), i.e., a mixture of the lysis reagent and a high salt reagent is achieved regardless of the order of addition of these two reagents. Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art to have reversed the steps of adding a high-salt solution before cell lysis. As stated in several Court decisions, changing the order of steps is prima facie obvious (see MPEP 2144.04.IV.C):

> *Ex parte Rubin*, 128 USPQ 440 (Bd. App. 1959) (Prior art reference disclosing a process of making a laminated sheet wherein a base sheet is first coated with a metallic film and thereafter impregnated with a thermosetting material was held to render *prima facie* obvious claims directed to a process of making a laminated sheet by reversing the order of the prior art process steps.). See also *In re Burhans*, 154 F.2d 690, 69 USPQ 330 (CCPA 1946) (selection of any order of performing process steps is *prima facie* obvious in the absence of new or unexpected results); *In re Gibson*, 39 F.2d 975, 5 USPQ 230 (CCPA 1930) (Selection of any order of mixing ingredients is *prima facie* obvious.).

12. No other references were found teaching or suggesting claims 24-28, 31-38, 40-49, 52-59 and 61-65, therefore these claims are allowed.

***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TERESA E. STRZELECKA whose telephone number is (571)272-0789. The examiner can normally be reached on M-F (8:30-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Primary Examiner, Art Unit 1637
November 21, 2009